**PATENT COOPERATION TREA.** 

# **PCT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 b	
02-029220PC	220) as well as, where applicable, new 3 below		
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)	
PCT/US 99/26772	09/11/1999	10/11/1998	
Applicant			

02-029220PC	ACTION	zo, ao wan ao, wilata appinaasia, nami o salam
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/US 99/26772	09/11/1999	10/11/1998
MAXYGEN, INC. et al.		
This International Search Report has been according to Article 18. A copy is being tra		nority and is transmitted to the applicant
	a copy of each prior art document cited in this	report.
language in which it was filed, unl	international search was carried out on the basess otherwise indicated under this item.  as carried out on the basis of a translation of the	
Authority (Rule 23.1(b)).  b. With regard to any nucleotide an was carried out on the basis of the contained in the internation filed together with the internation furnished subsequently to the statement that the subsequent application a	d/or amino acid sequence disclosed in the ine sequence listing: nal application in written form. rnational application in computer readable form this Authority in written form. this Authority in computer readble form. rsequently furnished written sequence listing displied has been furnished.	ternational application, the international search
2. X Certain claims were fou	nd unsearchable (See Box I)	
3. Unity of Invention is lac	king (see Box II).	
	bmitted by the applicant. hed by this Authority to read as follows: -BISPHOSPHATE CARBOXYLASE/0	XYGENASE
5. With regard to the <b>abstract,</b> The text is approved as sue the text has been establis within one month from the	bmitted by the applicant. hed, according to Rule 38.2(b), by this Authori e date of mailing of this international search re	ty as it appears in Box III. The applicant may, port, submit comments to this Authority.
6. The figure of the <b>drawings</b> to be pub as suggested by the appl because the applicant fai because this figure better	cant.	None of the figures.

#### INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/26772

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
UL 172	because they relate to subject matter not required to be searched by this Authority, namely:  Claims Nos.:  15–18 (incomplete) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark	The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.



### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15-18 (incomplete)

Present claims 15-18 relate to a polynucleotide comprising a gene characterised by the expression "shuffled", which describes a process of nucleic acid rearrangment that may either occur naturally during evolution (see Wolter F.P. et al., Plant Physiol., 1997, 114 (1), p.131-6) or may be carried out by man as claimed in present claims 1-9. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear and disclosed, namely those parts relating to a polynucleotide comprising a sequence encoding a Rubisco Form I L subunit gene shuffled by a method as claimed in claims 1-9 and linked to a selectable marker gene and further optionally linked to upstream and downstream flanking recombinogenic sequences, whereby said polynucleotide codes for an enzyme with a Km for CO2 (O2) which is significantly lower (higher) than the respective Km of any naturally-occurring rubisco enzyme.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

### INT RNATIONAL SEARCH REPORT

iternational Application No

PCT/US 99/26772

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N9/88 C12N15/29

C12Q1/68

C12N15/82

C12N5/14

C12P19/34

According to International Patent Classification (IPC) or to both national classification and IPC

#### **B. FIELDS SEARCHED**

 $\begin{array}{ll} \text{Minimum documentation searched } \text{ (classification system followed by classification symbols)} \\ IPC 7 C12N C12P C12Q \end{array}$ 

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

JUL 1 7 2000 TENT & TRAD

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SPREITZET R.J.: "GENETIC DISSECTION OF RUBISCO STRUCTURE AND FUNCTION" ANNUAL REVIEW OF PLANT PHYSIOLOGY AND PLANT MOLECULAR BIOLOGY, vol. 44, 1993, pages 411-434, XP000864484	1-4, 10-12, 15-18
X	page 412, line 15 - line 34 page 415, line 6 -page 423, line 42	15-18
Υ	WO 97 35966 A (MAXYGEN INC.) 2 October 1997 (1997-10-02)	1-4, 10-12,
	page 47, line 19 - line 22; claims 1,5,12-19	15-21
	-/	

Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
° Special categories of cited documents :	"T" later document published after the international filing date
"A" document defining the general state of the art which is not considered to be of particular relevance	or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another	involve an inventive step when the document is taken alone
citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the
"O" document referring to an oral disclosure, use, exhibition or other means	document is combined with one or more other such docu- ments, such combination being obvious to a person skilled
"P" document published prior to the international filing date but later than the priority date claimed	in the art.  "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
28 March 2000	12/04/2000
Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Schönwasser, D

## IN TRNATIONAL SEARCH REPORT

International Application No PCT/US 99/26772

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US 99/26772
Category °		
	passages	Relevant to claim No.
Y	LARIMER F.W. ET AL.: "Rhodobacter capsulatus Calvin cycle carbon dioxide fixation operon: fructose-1,6-/sedoheptulose-1,7-bisphosphate aldolase (cbbA) gene, partial cds, Form II ribulose-1,5-bisphosphate carboxylase/oxygenase (cbbM) gene, complete cds, and Calvin cycle operon: pentose-5-phosphate-3-epimerase (cbbE), etc."  EMBL DATABASE ENTRY RC23145; ACCESSION NO. U23145,14 April 1995 (1995-04-14), XP002132955	19-21
	CRAMERI A ET AL: "DNA SHUFFLING OF A FAMILY OF GENES FROM DIVERSE SPECIES ACCELERATES DIRECTED EVOLUTION" NATURE, vol. 391, 15 January 1998 (1998-01-15), pages 288-291, XP000775869 ISSN: 0028-0836 page 288, column 2, line 24 - line 28 page 289, column 1, line 4 -page 290, column 1, line 2	1-26
	JAMET E. ET AL.: "Genes encoding the small subunit of RUBISCO belong to two highly conserved subfamilies in Nicotianeae" JOURNAL OF MOLECULAR EVOLUTION, vol. 33, no. 3, September 1991 (1991-09), pages 226-236, XP000864454 the whole document	1-26
	WOLTER F.P. ET AL.: "rbcS genes in Solanum tuberosum: Conservation of transit peptide and exon shuffling during evolution" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 85, February 1988 (1988-02), pages 846-850, XP000877412	1-26
	FLACHMANN R. ET AL.: "Mutations in the Small Subunit of Ribulose-1,5-Bisphosphate Carboxylase/Oxygenase Increase the Formation of the Misfire Product Xylulose-1,5-Bisphosphate" PLANT PHYSIOLOGY, vol. 114, no. 1, May 1997 (1997-05), pages 131-136, XP000877382	1-26

#### IN 'RNATIONAL SEARCH REPORT

information on patent family members

International Application No PCT/US 99/26772

Patent document cited in search repor	t	Publication date		Patent family member(s)	Publication date
WO 9735966	Α	02-10-1997	US	5837458 A	17-11-1998
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			CA	2247930 A	02-10-1997
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			AU	713952 B	16-12-1999
			AU	1087397 A	19-06-1997
			CA	2239099 A	05-06-1997
			EP	0876509 A	11-11-1998
			EP	0911396 A	28-04-1999
			JP 2	000500981 T	02-02-2000
			WO	9720078 A	05-06-1997

